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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,587	08/20/2003	Connie Sanchez	05432/100M919-US4	5266

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EXAMINER	
ISSAC, ROY P	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,587	SANCHEZ ET AL.	
	Examiner	Art Unit	
	Roy P. Issac	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 20-34 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 20-34 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/06,6/05,9/04,1/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This application claims priority under 35 U.S.C 119 from foreign filed application PA 2001 00684, filed May 1, 2001. This Office Action is in response to applicant's application filed on 8/20/2003. The preliminary amendment filed on 1/05/2004 was entered into the application. Accordingly, claims 1-19 have been cancelled, and new claims 20-34 have been added.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20, the only independent claim in the application, is directed towards the use of escitalopram in a daily dose of 10mg or less. The specification does not define "less." The lack of lower limit in the claimed range renders the claim indefinite. Claims 21-34 are rejected due to their dependence from claim 20.

Claim 21 is further rejected under 35 U.S.C 112, second paragraph, for the following reason. Claim 21 is directed to a method for obtaining an effect in the patient after one week of administering escitalopram. Claim 21 does not point out which effect is obtained by the administration of drug one week in advance. The specification does not clearly define the effect obtained after one week.

Claim 22 is further rejected under 35 U.S.C 112, second paragraph, for the following reason. Claim 22 is directed to the use of a daily dose of 7.5mg or less of escitalopram. The specification does not define "less." The lack of lower limit in the claimed range renders the claim indefinite.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 20, 22-25. 27-30 and 32-24 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 22, 24-29, 31-33, 36 and 38-40, respectively of copending Application No. 10/644579. This is a

provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21,23,25,27,29,31,33,35 and 37 of copending Application No. 10/644588. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending applications are directed to the use of 10mg or less of escitalopram for the treatment of depression.

The '588 application is directed to treating severe depression in patients with escitalopram and its salts, in particular oxalate salts in dosage levels of

10mg or less. The instant patent application is directed to treating patients with depression who have sleep disturbances when treated with an SSRI other than escitalopram with escitalopram and its salts, in particular oxalate salts in daily dosage levels of 10mg or less. Sleep disturbances are well known to be associated with depression and the treatment of severe depression will include those with sleep disturbances associated with depression. It would have been obvious to one of ordinary skill in the art to use escitalopram to treat major depression and those with sleep disturbances due to depression.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 20-34 are further, provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 36-46 of copending Application No. 10/468685. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '685 application describes the treatment of major depression disorder with 2.5-10mg doses of escitalopram and its oxalate salts. The instant application is directed to the use of 10mg or less escitalopram for the treatment of patients who have sleeping disturbances when treated with a SSRI other than escitalopram without inducing sleep disturbances. Sleep disturbances are well known to be associated with depression and the treatment of major depression will include those with sleep disturbances associated with depression. It would have been

obvious to one of ordinary skill in the art to use escitalopram to treat major depression and depression that has sleep disturbances as one of its symptoms.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20, 22, 24, 25, 27, 29-32 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Boegesoe et. al., U.S. Patent # RE 34,712, or Boegesoe et.al, EP Publication # 0347066 B1, 1995 (PTO-1449, References included by the applicant).

The application is directed to a method for treating patients suffering from depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances. Claim 20, 22 and 24 describes the use of esctialopram in daily doses of 10mg or less, 7.5mg or less, and 5mg, respectively. Claim 25, 27 and 29 are directed towards the use of oxalate salt of escitalopram, while claims 30-32 and 34 describes the use of oxalate salt in crystalline form. Escitalopram is one of the

enantiomers of the well known antidepressant citalopram. (Specification, Page 1, lines 3-5). Escitalopram is also known by the name (+)-ctialopram.

The '712 patent describes the synthesis and use of (+)-citalopram for depression. (Column 1, lines 13-35). The '712 patent discloses a method for using (+)-citalopram and its non-toxic addition salts, such as oxalate salt, and crystallization. (See Column 1, line 45-46). The '712 patent further teaches the use of a pharmaceutically effective amount of (+)-citalopram and discloses 5-50mg daily dosage, in particular 5mg. (See example at Column 9, line 10).

It is well known that selective serotonin reuptake inhibitors (SSRI) are used in treating depression. Low dose levels are well known to give reduced side effects.

Claims 20, 22, 24, 25, 27, 29-32 and 34 are rejected under 35 U.S.C 102(b) as anticipated by Boegesoe, et. al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21, 23, 26, 28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boegesoe et.al. (U.S. Patent # RE 34,712) or Boegesoe et.al, (EP Publication # 0347066 B1, 1995) in view of Bouchard et.al. (PTO-1449, References included by the applicant).

The '712 patent discloses a method for using (+)-citalopram and its non-toxic addition salts, such as oxalate salt, and crystallization. (See Column 1, line 45-46). The '712 patent further teaches the use of a pharmaceutically effective amount of (+)-citalopram and discloses 5-50mg daily dosage, in particular 5mg. (See example at Column 9, line 10)

Boegesoe et. al. does not expressly disclose that daily dose is administered to obtain an effect in the patient after one week (claim 21), and the daily dose is 7.5mg (claim 23) herein.

Bouchard et.al. teach the use of citalopram because of its low side effects in patients with depression. The authors note that; "Single MADRS-items analyses revealed a better effect of citalopram on "reduced appetite" on day 14 and 42, "apparent sadness", "reduced sleep" and "suicidal thought" on day 42." (Pg. 57, Col1, lines 32-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a daily dose of 5-10mg, such as 7.5mg, of (+)-citalopram or its oxalate salt for the treatment of patients suffering from depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances.

One of ordinary skill in the art would have been motivated to treat patients with (+)-citalopram in daily dosage ranges of 5-10mg, including 7.5mg, for patients suffering from depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances, because citalopram has advantages as an antidepressant with low sleep disturbance and because citalopram's pharmacological activity is attributed to its (+)-citalopram enantiomer. The instant claimed range of 10mg or less overalps with the 5-50mg disclosed in Boegesoe. If the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exits. See *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir 1990). See MPEP § 2144.05 [4-1]. Thus, the claimed invention as a whole is clearly *prima facie* obvious over the combined teachings of the prior art.

Claims 20-34 are further rejected under 35 U.S.C. 103(a) as being unpatentable over Feighner, JP et. al. (PTO-892, Reference included by the examiner), in view of Hyttel, J. et. al. (PTO-1449, Reference included by the

applicant) further in view of Bouchard et. al.(PTO-892, Reference included by the examiner).

Feighner et. al disclose the use of racemic citalopram for moderate-to-severe depression in dosage levels ranging from 10mg to 60mg. One skilled in the art would recognize that a racemic mixture contains two enantiomers of a compound in its (+) and (-) form. The (+) and (-) designate the optical activity of the compound. Generally, a racemic mixture has both enantiomers in about equal proportions. Thus, a 10mg dose of racemic citalopram should contain 5mg of its (+) enantiomer and 5mg of its (-) enantiomer. The chiral dosage range of (+)-citalopram in Feigner's study is estimated to be 5-30mg. The authors also disclose the use of citalopram in patients who have been treated with other antidepressants. (Page 826, Table 1, line 6). The study also shows a decrease in insomnia in patients treated with citalopram at lower dose levels. (Page 828, Table 3, line 3). The length of the study was six-weeks. (Page 824, Column 1, Paragraph 3).

Feighner et. al. does not disclose the use of the escitalopram ((+)-citalopram), as the applicant define that esctialopram refers to one of the enantiomers of *S*- or (+)-citalopram. (Specification, Page 1, line 3-5). Feigner et. al. does not disclose the use of oxalate salt or the oxalate salt in its crystalline form.

Hyttel et. al teach the use of (+)-citalopram, and its crystallized oxalate salt, and shows that the pharmacological activity of the racemic citalopram is

attributed to one of its enantiomers, (+)-citalopram, also known as escitalopram. (See Pg.157, lines 10-14, and Pg. 158, lines 25-29).

Schoffers et. al teach the advantages of using chirally pure compounds as pharmaceuticals. The author notes: "An increasing interest in understanding biological processes and the general recognition that chirality plays a crucial role in nature fostered tremendous effort in enantioselective synthesis. In the course of synthesizing natural products and designing new target compounds, chemists had to acknowledge the fact that enantiopurity is related to biological processes. Opposite enantiomers interact differently within an organism and can display various activities." (See Page 3770, lines 3-12). Furthermore, the advantages of using chirally pure drugs are well known in the art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a daily dose of 5-10mg of (+)-citalopram or its oxalate salt for the treatment of patients suffering from depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances.

One having ordinary skill in the art would have been motivated to treat patients with depression who have sleep disturbances when treated with a selective serotonin reuptake inhibitor other than escitalopram without inducing sleep disturbances comprising administering a daily pharmaceutically effective amount of escitalopram, because decreasing dose levels in citalopram leads to reduced side effects, and it is effective in daily dose ranges of 10-60mg or 5-30mg of (+)-citalopram. One skilled in the art would be further motivated to use

(+)-citalopram or its oxalate salt because of the advantages of using a chirally pure drug and due to Hyttel's showing that the pharmacological activity resides in (+)-citalopram enantiomer. The instant claimed range of 10mg or less overalps with the 10-60mg (5-30mg chiral dosage) disclosed in Feigner. If the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exits. See *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir 1990). See MPEP § 2144.05 [4-1]. Thus, the claimed invention as a whole is clearly *prima facie* obvious over the combined teachings of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

5/10/06

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April 28, 2006

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